An Endowed Professorship Ensures Leadership for WHRY

We are pleased to announce that, based on the extraordinary generosity of donors, funding is now placed in Yale’s endowment that will generate a permanent resource in support of a professorship for the Director of Women’s Health Research at Yale.

Approved by the Yale Corporation, the professorship is named the Norma Weinberg Spungen and Joan Lebson Bildner Professor as a tribute to the mothers of the leadership donors – Elisa Spungen Bildner, Yale ’75, and Robert Bildner, Yale ’72. This important gift complements gifts from other donors and a foundation that chose to remain anonymous.

Yale University President Peter Salovey and Fellows of the Corporation voted to appoint Carolyn M. Mazure, Ph.D., who has been Director since founding our Center in 1998, as the inaugural Norma Weinberg Spungen and Joan Lebson Bildner Professor as a tribute to the mothers of the leadership donors – Elisa Spungen Bildner, Yale ’75, and Robert Bildner, Yale ’72. This important gift complements gifts from other donors and a foundation that chose to remain anonymous.

“This honor means a great deal to me personally, and provides institutional recognition of the need for and value of research on women’s health and gender differences,” Mazure said. “There is so much more to be done, and I thank the donors for ensuring that our Center has a solid platform to always pursue this vitally important work.”

Much More Work to be Done!

- What the endowed professorship means for our Center’s future – p. 8
- “Keep the Momentum Going” – p. 9
- A gallery of photos from the professorship naming event – p. 10
JOIN THE SOCIETY OF FRIENDS

Consider a donation to Women’s Health Research at Yale in celebration of a birthday, a special occasion, or to honor someone in your life.

Our Society of Friends ensures the future of Women’s Health Research at Yale. Gifts are welcome at all levels.

To make an online gift visit www.yalewhr.org or mail your gift to Women’s Health Research at Yale P.O. Box 208091 New Haven, CT 06520-8091

Educational and outreach activities are made possible through the generous support of:

- The Community Foundation for Greater New Haven
- The Grace J. Fippinger Foundation
- Maximilian E. & Marion O. Hoffman Foundation, Inc.
- Seymour L. Lustman Memorial Fund
- The Werth Family Foundation
- Anonymous Donors

Women’s Health Research at Yale was founded in 1998 with initial funding from The Patrick and Catherine Weldon Donaghue Medical Research Foundation.

In honor of…
Susannah Bailin • Elizabeth Green • Dr. Sharon Karp
Dr. Roslyn Milstein Meyer • Carol Ross • Patti Russo

Allison Jacobs’ admittance to the Bar
Linda Lorimer’s CT Women’s Hall of Fame induction
Lili Jaubert’s birthday
Dr. Mark Schpero’s birthday
Cancer survivors and those fighting the fight

In memory of…
Dr. Judith Barr • Birgitta W. Johnson
Dr. Morton J. Weyler

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Understanding Cellular Mechanisms that Underlie Gender Differences In Aging and Neurodegenerative Diseases

The incidence, onset and course of disorders involving degeneration of brain nerve cells (neurons) – such as Alzheimer’s disease and Parkinson’s disease – have consistently shown gender differences.

Women, for example, have a higher incidence, earlier onset and more severe dementia in Alzheimer’s disease than men. By contrast, men have a higher incidence and earlier onset of Parkinson’s disease, often with different symptoms than women.

The reasons for these differences remain largely unknown. Recently emerging evidence indicates that estrogen plays a pivotal role. Before menopause, levels of this hormone help protect women against neurodegenerative processes. After menopause, it appears that decreasing levels of estrogen contribute to the risk of cognitive decline and Alzheimer’s disease.

Little research, however, has focused on the cellular mechanisms underlying gender differences in normal and pathological aging. Further, no research has examined the role of a type of brain cell called astroglial cells in gender differences in aging, despite a clear role for these cells in the generation and preservation of neurons, and evidence that these cells facilitate estrogen’s role in supporting healthy cells.

Using a Women’s Health Research at Yale Pilot Project Program grant awarded in 2012, Dr. Flora Vaccarino, Professor of Neurobiology and Harris Professor in the Child Study Center, examined these astroglial cells in relation to aging and degeneration of neurons in laboratory research with female and male mice.

Specifically, she charted changes in neurons and connections between these cells across the lifespan, and the role that particular astroglial cells, called astrocytes, play in the healthy development and degeneration of neurons.

Her project represents initial steps toward understanding the cellular mechanisms involved in gender differences in aging, as well as in neural degeneration in disorders such as Alzheimer’s disease. By illuminating these cell mechanisms, Vaccarino expects to lay the groundwork for identifying new targets in developing interventions for neurodegenerative diseases, paying particular attention to gender effects and possible gender-specific approaches.

Vaccarino earned her medical degree from Padua University in her native Italy and studied neuropharmacology and cell biology as a research fellow at the National Institutes of Health, before starting her residency in psychiatry at Yale. Now with an endowed professorship, she studies mouse and human neural stem cells (self-renewing cells that can differentiate and become new nerve cells) and their role in neuronal development and repair. She and a group of colleagues recently founded the Program in Neurodevelopment and Regeneration to harness the power of stem cells for understanding individual variation in neurodevelopment and the physiological processes at work in neuropsychiatric disorders.

Astrocytes help nerve connections function

In her WHRY-funded study, Vaccarino has focused much of her attention on astrocytes because these astroglial cells play important roles in the development and maintenance of healthy neurons and the connections between them, called synapses. These are not physical junctions, but rather gaps between nerve endings across which information is

(Continued on page 4)
conveyed by chemical or electrical signals. These interactions between neurons enable people to think, move, feel emotions, and maintain stability in the body’s various systems.

These astrocytes, which are the most abundant cells in the brain, surround the neuronal connections, acting like glue to hold them together structurally, according to Vaccarino. In addition, these enveloping astrocytes help regulate the transmission of electrical impulses, nourish neurons, store and release energy (as glycogen) to fuel the nerve cells, and remove and recycle unwanted, tiny pieces (molecules) of nerve cells.

In some regions of the adult brain, healthy astrocytes function as neural stem cells that can become more stem cells, generate more neurons, or prompt the growth and regeneration of neurons that, in turn, contribute to healthy neuronal connections. Dysfunction of these astrocytes triggers neuronal death in neurodegenerative disorders, according to Vaccarino.

“These are very important cells,” she said. “So we were interested in seeing how astrocytes change as nerve cells develop in the early post-natal period and mature, with a particular emphasis on what happens in aging.”

**Enrichment promotes healthy nerve connections**

During the lifespan, neuronal connections exhibit what neuroscientists call plasticity. They are malleable and dynamic – growing, changing, adapting, strengthening, withering, ceasing to function, or dying. The number of neuronal connections, or synapses, changes across the lifespan as well, increasing in young age and decreasing in adulthood. All of these changes, which are greatest during brain development just after birth, are driven by a genetic blueprint and, importantly, by life experiences, as learning takes place and memories are formed.

Previous research suggests that enriching experiences, such as learning a language, playing a musical instrument, honing athletic skills, or solving math problems, promotes the development, maturation and strengthening of neuronal connections. “Enrichment does a lot of good things,” Vaccarino said. “It increases plasticity, has beneficial effects on aging, increases the brain’s ability to repair nerve cell damage from injury, and enhances the capacity for learning – all by beneficial effects on neuronal connections.”

In her laboratory study, Vaccarino examined the functioning and fate of astrocytes in juvenile, young adult and aging mice. Some of the mice were in an enriched environment – with toys, exercise, and other mice with which to interact – and some of the mice were without enrichment – simply sitting in their cages. Before receiving her WHRY pilot grant, Vaccarino had anticipated conducting a study on glial cells in aging by comparing only male mice in enriched and non-enriched environments.

“What the grant has allowed us to do is add the essential component of the story – to compare females and males in the enriched and non-enriched environments,” Vaccarino said. Because female hormonal cycles add complexity and variability, using female animals adds expense and increases data collection work. However, by studying females, the research is most relevant for understanding cellular mechanisms at work in aging women.

(Continued on page 5)
Finding gender differences in enrichment effects

Her study includes two main aims: examining astrocytes to understand the cellular mechanisms that underlie gender differences in aging, and identifying genes expressed in astrocytes and involved in aging. (Genes are forms of DNA, deoxyribonucleic acid, that carry instructions for making proteins, the building blocks of cells. Gene expression is the process by which information from a gene is used to make proteins.)

Although she is still analyzing the very complex data she collected, Vaccarino said she found gender differences in the effects of enrichment on astroglial cells. “This is preliminary but female mice have an accelerated, increased effect of enrichment that affects neuronal differentiation (when astrocytes/neuronal stem cells can become either more stem cells or develop into nerve cells), particularly at younger ages. And we found genes that are regulated by gender differences, and are affecting astrocytes in both the process of making more stem cells, and becoming mature nerve cells,” she said.

“I believe we are tapping into something significant, because I was quite surprised to see differences,” Vaccarino said.

Not surprisingly, gender differences faded in very old mice, said Vaccarino, most likely because of the loss of estrogen in the aging females.

Targeting genes for developing interventions

By identifying genes that are modulated by gender, Vaccarino ultimately hopes to target particular genes that control brain nerve cell development and play roles in determining gender differences in neurodegenerative diseases. Identifying such targets will pave the way for developing gender-sensitive interventions for disorders including Alzheimer’s and Parkinson’s diseases.

Vaccarino cautions that her study showed that between 300 and 400 genes exhibited changes affected by gender in the mice reared in the enriched environment. The sorting of these genes has just begun, she said, and will take considerable time and effort. But this initial project has allowed her to begin charting gender differences in an area related to women’s health and aging that has received little attention. Her results will enable her to refine and further her search for appropriate intervention targets. In sum, she is off to a great start.

“We are grateful we were able to look at gender differences,” Vaccarino said. “Without this funding, we would not have found them.”

Terminology & Definitions

Neurodegenerative Disorders: Umbrella term for diseases involving progressive loss of structure or function of brain nerve cells (neurons), such as Alzheimer’s and Parkinson’s diseases.

Astrocytes: Also called astroglial cells, these most abundant brain cells play key roles in the development and function of neurons, and facilitate estrogen’s role in supporting healthy brain nerve cells.

Estrogen: A female sex hormone produced mainly by the ovaries and essential in inducing menstrual/estrus cycles. Evidence suggests estrogen helps maintain healthy neurons, and loss of estrogen after menopause can contribute to neurodegenerative processes.

Why can’t estrogen be used to prevent or treat post-menopausal women with neurodegenerative diseases?

Once brain nerve cells are unhealthy, it is hypothesized that these cells will not benefit from estrogen exposure. If initiated when a woman is transitioning to menopause, estrogen therapy may have a beneficial effect only if neurological decline has not occurred – the so-called healthy cell bias hypothesis. Thus hormone therapy with estrogen still holds promise for maintaining cognitive function and memory in women with healthy brain cells.

The Women’s Health Research at Yale Pilot Project Program is supported in part by the Maximilian E. and Marion O. Hoffman Foundation, the Seymour L. Lustman Memorial Fund, The Seedlings Foundation, The Werth Family Foundation, and anonymous donors.
BIRCWH Scholars Becoming Independent Investigators in Women’s Health Research

Four junior faculty scholars are successfully completing their scientific training in our NIH-funded Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) program and will soon be graduating from the program to pursue research careers.

Through the BIRCWH program, which provides intensive training, mentoring, coaching and team science experience, our Center is meeting a long-term need in preparing emerging scientists in methods and research design that enable them to become the next generation of scientists studying women’s health and gender differences.

“We’re so pleased to have promising scientists come to us to study as junior faculty, and it’s been our great pleasure to integrate them into our Center,” said WHRY Director Dr. Carolyn Mazure.

The five-year BIRCWH grant, awarded in 2011 to Mazure as Principal Investigator, and Samuel Ball, Ph.D. as Research Director, established this program to train exceptional junior faculty interested in a research career focused on women’s health as it relates to addictive behaviors. This $2.5 million grant is funded by the National Institutes of Health Office of Research on Women’s Health, the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism.

Among the BIRCWH Scholars, Dr. Tomoko Udo is examining biology and behavior that may underlie the obesity epidemic. During the last year, she also has competed successfully for an external grant from the Foundation for Alcohol Research to study the relationship between a hunger-stimulating hormone and alcohol use disorders, and whether this relationship differs by gender and smoking status. Her BIRCWH-supported research has been published in multiple journals, and recognized in mainstream media by the online Connecticut Health Investigative Team and The Hartford Courant newspaper, (“For Comfort Food, Is Gender Destiny?” September 23, 2013).

Dr. Elise DeVito is studying the relationship between sex hormones and impulsivity in addictive behaviors. She has presented her BIRCWH-supported research at conferences across the country and her work has been recognized in high-impact scientific journals. Among the acknowledgments of her work, she has won a travel award from the National Institute on Drug Abuse to present her research at the annual meeting of the American Psychological Association, and she is currently submitting funding proposals to the National Institute on Drug Abuse.

Dr. Azure Thompson is exploring smoking behaviors, particularly patterns of initiation and quitting among young black women. She has won travel awards from the National Institute on Drug Abuse and the Society of Research on Nicotine and Tobacco to present her research, and most recently has competed successfully for the Kaiser Permanente Burch Minority Leadership Development
Award to continue her progression toward leadership in her research and subsequent implementation of her findings to improve minority health.

Dr. Megan Smith is developing new interventions for mood and substance use disorders in collaboration with the New Haven community to improve the health of mothers and their children. As with all the research we support, the BIRCWH research projects emphasize generating findings with practical benefits. With regard to Smith’s work, she leads a unique effort in which she designed a smartphone app, called Momba – which interfaces with Facebook, for new mothers to form support networks. Using BIRCWH research funding for the initial design of the intervention, she has now obtained continued funding from the National Institute of Mental Health. Ultimately, her plan is to use the intervention nationwide to help new mothers prevent depression. In addition to multiple external grants to further her research, her work is now recognized in several scientific journals. Her community-based intervention has been featured by several media outlets, including The New Haven Register, (“New phone app aims to aid New Haven mothers with depression,” July 31, 2012).

When she began her BIRCWH training, Smith had prior experience in psychiatric epidemiology. “But I did not have training in developing interventions in the community. By being part of this program, I now have had the mentoring to take key concepts from social and psychiatric epidemiology and apply those to tailored interventions for women dealing with depression and addiction,” Smith said. “The BIRCWH training has launched my career as an independent investigator.”

A new group of BIRCWH scholars will arrive next year, as applications are being accepted for positions that will begin July 1, 2014.

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**Investigator News...**

**Arnsten Wins NIH Pioneer Award**

Dr. Amy Arnsten, Professor of Neurobiology and of Psychology, and a WHRY-funded investigator, was a recipient of a National Institutes of Health Pioneer Award. This award, announced in September, is given to researchers of exceptional creativity.

Her award is one of 78 grants for innovative research under the NIH’s High Risk-High Reward program. Arnsten will use the five-year $2.5 million grant to study how genetic and environmental factors interfere with the function of a highly-evolved region of the brain (the association cortex, essential for complex mental functions) to produce cognitive deficits in disorders including schizophrenia and Alzheimer’s disease.

As a WHRY-funded investigator, Arnsten demonstrated in laboratory models that the effects of stress on the pre-frontal cortex – the brain region that regulates thoughts, actions and emotions – are more pronounced in females than males.

Her findings provided a biological basis for why women compared to men are so much more reactive to stress-related depression.
Fifteen years ago, Women’s Health Research at Yale was founded to advance the study of women’s health and gender-specific approaches to healthcare.

Several weeks ago, our founding Director was named to a new endowed professorship providing enduring support for the leadership of Women’s Health Research at Yale.

With so much more work to be done in so many areas of women’s health research, this professorship inaugurates a permanent institutional structure for pursuing our mission, at a time when it is most needed. Federal funding for health research, not to mention research to advance gender-specific medicine, is being severely limited.

With your support and this academic research base now secured by the endowed professorship, we will dramatically expand scientific knowledge on women’s health and gender differences.

“The reason this professorship is so exciting is that it provides a fundamental building block to speed the generation of biomedical research findings that will improve the health of the nation,” said Carolyn Mazure, Ph.D., recently named the Norma Weinberg Spungen and Joan Lebson Bildner Professor for Women’s Health Research at Yale.

As people learn about the impact of the endowments we recently received, they may wonder what role their gift plays in our work and future. “The answer,” according to Mazure, “is that individual gifts have been the bedrock of our Center and continue to be essential in supporting our operations and research initiatives.”

Specifically, continued support will enable our Center both to maintain and grow our thriving programs that:

🔹 Initiate highly inventive, never before undertaken studies on women’s health and gender differences involving a host of crucially important women’s health conditions.

🔹 Forge collaborative research consortia to bring scientists from varying disciplines together to tackle the most challenging, emerging questions in women’s health.

🔹 Train and mentor a new generation of women’s health investigators who can infuse the study of gender differences and the practice of gender-specific medicine into the wider medical landscape.

🔹 Disseminate our research findings and relevant health information to members of the community through educational outreach.

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Dr. Mazure speaks at the November 4th Professorship Celebration.

President Peter Salovey, Dr. Mazure, & Marta Moret

Yale School of Medicine Dean Robert Alpern, Eliza Spungen Bildner, Marjorie “Kitty” Northrop Friedman & Robert Bildner
A year ago we began celebrating the 15th anniversary of the founding of Women’s Health Research at Yale. And what an incredible difference this year has made.

We are now celebrating Dr. Mazure’s being named the inaugural Norma Weinberg Spungen and Joan Lebson Bildner Professor. This endowed professorship for the Director of Women’s Health Research at Yale provides enduring support for the leadership of our center, and affirms 15 years of turning inventive health research findings into improvements in women’s health – a much deserved honor.

I want to thank all of our donors for their visionary generosity. Their giving points the way toward dramatically expanding our Center’s ability to make gender-specific medicine a routine part of healthcare.

With your support, we could fund the next pivotal study on a disorder that affects the women we know and love, and we can train another new women’s health investigator who will someday make a crucial discovery to improve the health of the women in our lives.

Let’s keep the momentum going!

With sustained commitments, our Center’s future promises to be much brighter. Please Give to Women’s Health Research at Yale – and become part of an even bigger success story.

And remember, momentum matters at all levels. Every gift makes a difference.

Thank you!
Yale School of Medicine announced the naming of Carolyn M. Mazure, PhD Director, Women’s Health Research at Yale as the inaugural Norma Weinberg Spungen and Joan Lebson Bildner Professor
4 November 2013
The Maurice R. Greenberg Conference Center New Haven, Connecticut

Photos: Clockwise from Top Left, L to R (1) Robert Bildner, Elisa Spungen Bildner (2) Marjorie “Kitty” Northrop Friedman, Carolyn M. Mazure, Susan Lustman Katz, Vice President Linda Koch Lorimer (3) Dr. Mazure, Marta Moret, President Peter Salovey (4) Dean Robert J. Alpern, Dr. Mazure, President Salovey (5) Dr. Mazure, Eve Hart Rice, Marta Moret (6) Douglas Karp, Marta Moret, President Salovey, Dr. Sharon Karp (7) Standing: Kim Healey, Dr. Anthony Koleske, Judge Susan Carney; Seated: Charles Ellis, Robert Bildner, Marna Borgstrom, Elisa Spungen Bildner, V.P. Linda Koch Lorimer (8) Dr. Mazure, Wendy Naratil, President Salovey, Thomas Naratil (9) Kitty Friedman, Dr. Mazure (10) Guest reception
Council News...

Wendy Naratil Joins Council

Wendy Underwood Naratil, a Yale College ’83 graduate, is the newest member of the Women’s Health Research at Yale community advisory Council. Wendy and her husband Tom – also a Yale ’83 graduate, live in New Jersey and have five children including twin daughters, Valerie and Stephanie – who are Yale College graduates, class of 2011. She has had a longstanding interest in women’s health research, and the couple recently provided a class reunion gift to endow WHRY’s new Wendy U. and Thomas C. Naratil Pioneer Award. This important Pioneer Award will exist in perpetuity and be granted annually to WHRY investigations that are highly inventive, or close to a major breakthrough but need funding to reach their aim. It is a pleasure to welcome Wendy to the Council for Women’s Health Research at Yale.

CT Women’s Hall of Fame Inducts Linda Lorimer, Rosa DeLauro

Linda Koch Lorimer, J.D., Vice President of Yale University and Special Advisor to our Council, and U.S. Representative Rosa DeLauro of New Haven, an Honorary Member of our Council, were among four women inducted into the CT Women’s Hall of Fame on November 6th.

WHRY Director Carolyn Mazure, Council members and spouses, and WHRY staff added their standing ovations for these two leaders at the organization’s 20th anniversary induction ceremony, focusing this year on “Women’s Education – Women’s Empowerment.”

Press Notes...

As We Age, Diet Can Really Matter

If you believe that eating right can help limit chronic diseases and cognitive decline late in life, take a look at two separate studies published in October and November.

The first, a Yale-led study published in the journal Cell Metabolism and summarized in YaleNews October 21st, suggests it may be possible to develop diets to dampen inflammation processes as a means to prevent chronic age-related diseases.

The second, published in the Annals of Internal Medicine and reported by National Public Radio November 5th, found that women in their 50s who followed a Mediterranean-style diet rich in fish, nuts, vegetables and fruit were about 40 percent more likely to reach their later decades without developing chronic diseases and memory or physical problems, compared to women who didn’t eat this way.

“For all of us nearing middle age, or slogging through it, yes, there is a benefit in eating...” a healthy diet, the NPR report stated.

I hope you all enjoy the holiday season – but at the risk of sounding like Scrooge – try to watch what you eat!
Women’s Health Research at Yale
Wishes you and your loved ones a Joyous Holiday Season and a Healthy 2014.

Generating research findings to improve well-being.